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| 10/789,835      | 02/27/2004  | Todd A. Thompson     | 960296.00516        | 8254             |

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| EXAMINER |
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ANDERSON, JAMES D

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| ART UNIT | PAPER NUMBER |
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1614

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06/20/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |  |  |
|------------------------------|--------------------------------------|--|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/789,835 | <b>Applicant(s)</b><br>THOMPSON ET AL. |  |
|                              | <b>Examiner</b><br>JAMES D. ANDERSON | <b>Art Unit</b><br>1614                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 March 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,5,6,8,9 and 11-24 is/are pending in the application.
- 4a) Of the above claim(s) 11-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,5,6,8 and 9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/10/2008</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

#### ***Claims 1-2, 5-6, 8-9, and 11-24 are presented for examination***

Applicants' amendment filed 3/10/2008 has been received and entered into the application. Accordingly, claims 1-2, 5-6, and 8-9 have been amended and claim 4 has been cancelled.

Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

#### ***Election/Restrictions***

Claims 11-24 remain withdrawn from consideration as being drawn to non-elected subject matter per Applicants' response filed 12/5/2006. Accordingly, claims 1-2, 5-6, and 8-9 are presently under examination and are the subject of this Office Action.

#### ***Information Disclosure Statement***

Receipt is acknowledged of the Information Disclosure Statement filed 3/10/2008. The Examiner has considered the references cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

***Response to Arguments***

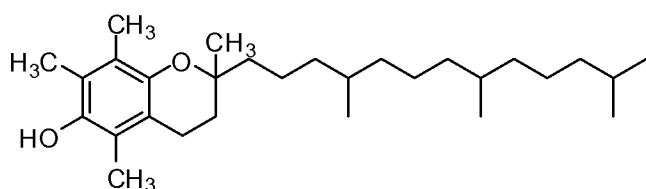
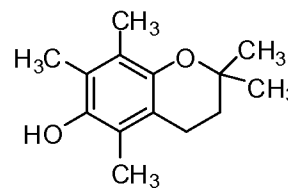
Applicant's arguments filed 3/10/2008 have been fully considered and are persuasive in part. Rejections not reiterated from the previous Office Action are withdrawn.

Firstly, with respect to the 35 U.S.C. 112, 1<sup>st</sup> Paragraph (Enablement) rejection of claims 1, 4-5, and 8-9 (now 1-2, 5-6, and 8-9), Applicants' arguments are persuasive that the claims are enabled for inhibiting the growth of androgen-dependent prostate cancer tumor cells or delaying the progression of androgen-dependent prostate cancer comprising administering the claimed compounds to a patient having prostate cancer tumor cells or prostate cancer. However, the Examiner is not persuaded that the claims are enabled to the extent that the claims read on the prevention of prostate cancer. The instant claims have been amended in a manner such that it is not clear that the administration step of the instant claims only comprises administration to a patient *having* a prostate cancer tumor. In other words, the claims as amended encompass administering the claimed compounds to any patient. Accordingly, the claims are herein rejected for the reasons of record to the extent that the claims read on the prevention of androgen-dependent prostate cancer (*i.e.*, administration of the claimed compounds to any patient).

Secondly, with respect to the 35 U.S.C. 103 rejection of claims 1, 2, 5, and 6 as being unpatentable over Gunawardena *et al.* in view of Sheu *et al.*, Applicants argue that PMC is not disclosed in Gunawardena *et al.* and that growth inhibition of androgen dependent cell lines does not logically or predictably mean that the inhibitory compound is an anti-androgenic. Accordingly, Applicants assert that Gunawardena teaches away from the claimed invention by suggesting that a-tocopherol lacks anti-androgen activity

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in comparison to other known antioxidants. With regard to the Sheu references, Applicants argue that Sheu provides no suggestion that PMCol can be used to inhibit growth of androgen-dependent prostate cancer tumor cells or delay progression of androgen-dependent prostate cancer. Applicants appear to acknowledge, however, that Sheu teaches that PMCol is 6-times more potent than  $\alpha$ -tocopherol on platelet aggregation and antioxidant activity. For the purposes of discussion, the Examiner is providing the chemical structures of  $\alpha$ -tocopherol (Vitamin E), as taught in Gunawardena, and PMCol, as taught in Sheu, below.

 **$\alpha$ -Tocopherol****PMCol**

Note that PMCol differs from  $\alpha$ -tocopherol in that the phytyl group of  $\alpha$ -tocopherol is replaced with a methyl group in PMCol. With regard to the teachings of the prior art, Gunawardena teaches that  $\alpha$ -tocopherol and other antioxidants (specifically PDTC and DETC) inhibit human prostate cancer cells through apoptosis. While Gunawardena is silent with respect to PMCol, Sheu teaches that PMCol is a more potent antioxidant than  $\alpha$ -tocopherol, the most potent inhibitor of nuclear factor-kB (NF-kB) activity among the  $\alpha$ -tocopherol analogues tested, is more hydrophilic than other  $\alpha$ -tocopherol derivatives, and has potent radical scavenging activity. As such, there are two things that connect the teachings of the cited references: 1) the fact that Gunawardena teaches that antioxidants inhibit prostate cancer cells through apoptosis and Sheu teaches that PMCol is a more potent antioxidant than tocopherol and 2) the fact that PMCol is structurally related to

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tocopherol. Since all three antioxidants were effective in inhibiting prostate cancer cells to some extent and PMCol is a more potent antioxidant than tocopherol, the skilled artisan would reasonably expect PMCol to inhibit prostate cancer cells with at least the same efficacy as tocopherol. The fact that Applicants discovered another mechanism through which PMCol might inhibit prostate cancer cells is not pertinent to the present rejection because the cited prior art suggest and motivate the administration of PMCol to inhibit prostate cancer cell growth.

***Claim Rejections - 35 USC § 112 (2<sup>nd</sup> Paragraph) – New Grounds of Rejection***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 5-6, and 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, it is not clear to whom or what the claimed compounds are being administered. While the preambles of claims 1-2, 5-6, and 8-9 recite methods of "inhibiting the growth of androgen-dependent prostate cancer tumor cells in a human" (claims 1 and 2); "delaying the progression of androgen-dependent prostate cancer in a human" (claims 5 and 6); and "preventing the recurrence of androgen-dependent prostate cancer in a human" (claims 8 and 9), the active method step of the claims is simply "administering" the claimed compound(s). The preamble of the claims is not so linked to the body of the claims so as to clearly convey that the administering step recited in the body of the claims necessarily requires administration to the patient population defined by the preamble of the claims (*i.e.*, a patient who has or

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has had prostate cancer). For example, in claim 1 one could administer the claimed compound to any patient, and such administration would naturally inhibit the growth of androgen-dependent prostate tumor cells in said patient, even if such tumor cells were not present in the patient (*i.e.*, the claims reasonably could be interpreted to read on the prevention of prostate cancer).

***Claim Rejections - 35 USC § 112 (1<sup>st</sup> Paragraph) – New Grounds of Rejection***

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 5-6, and 8-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting the growth of androgen-dependent prostate cancer tumor cells in a human *having* androgen-dependent prostate cancer tumor cells, or delaying the progression of androgen-dependent prostate cancer in a human *having* androgen-dependent prostate cancer, does not reasonably provide enablement for inhibiting the growth of androgen-dependent prostate cancer tumor cells or delaying the progression of androgen-dependent prostate cancer, or preventing the recurrence of androgen-dependent prostate cancer in patients not diagnosed as being in need of such treatment (*i.e.*, prevention). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

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To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by “undue experimentation,” the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).<sup>1</sup>

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

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<sup>1</sup> As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is “undue”, not “experimentation”.

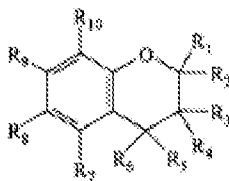
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These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The instant claims have been amended in a manner such that it is not clear that the administration step of the instant claims comprises administration to a patient *having* a prostate cancer tumor or prostate cancer. In other words, the claims as amended encompass administering the claimed compounds to any patient.

The invention relates to the treatment or prevention of androgen-dependent prostate cancer in a human patient comprising administering a compound having the structure:



wherein R<sub>4</sub> and R<sub>5</sub> are H; R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>9</sub> and R<sub>10</sub> are independently an unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl group; and wherein R<sub>8</sub> is an OH. Claims 8 and 9 relate to preventing the recurrence of androgen-dependent prostate cancer in a human patient.

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The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

That factor is outweighed, however, by the unpredictable nature of the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). As illustrative of the state of the art, the examiner cites Sausville *et al.* (Cancer Research, 2006, vol. 66, pages 3351-3354), Johnson *et al.* (British J. of Cancer, 2001, 84(10):1424-1431), and Singh *et al.* (Endocrine-Related Cancer, 2006, vol. 13, pages 751-778).

Singh *et al.*, also cited for evidentiary purposes, review the mechanism of action of novel agents for prostate cancer chemoprevention. It is noted that "chemoprevention" as used in Singh *et al.* relates to prevention, suppression, and/or reversal of early and/or

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late stages of cancer growth (page 751). Optimal therapeutic response in prostate cancer patients has been compounded by the problem of early diagnosis and with the emergence of androgen independence during commonly used anti-androgen therapy (Abstract).

While many agents have been tested for chemoprevention in prostate cancer patients, there is no known agent that can prevent prostate cancer from occurring (pages 767-768).

This article plainly demonstrates that the art of preventing prostate cancer, particularly in humans, is extremely unpredictable.

2. The breadth of the claims

The claims vary in breadth; some (such as claims 1, 5, and 8) are broad, encompassing the prevention of androgen-dependent prostate cancer with a genus of compounds. Others, such as claims 2, 6, and 9, are narrower, reciting a specific species of the claimed genus of compounds. All, however, are extremely broad insofar as they encompass the general prevention of androgen-dependent prostate cancer with the same compounds, only one of which has actually been tested for inhibiting the growth of existing prostate cancer tumors.

3. The amount of direction or guidance provided and the presence or absence of working examples

Firstly, it is noted that the present invention is based on the inventor's discovery that the chromanol-derived moiety of vitamin E possesses potent anti-androgenic activity in androgen-dependent cells (page 5, lines 11-13). In this regard, one compound was shown to have such activity. This compound, 2,2,5,7,8-pentamethyl-6-chromanol

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(PMCol), is a commercially available compound known for its antioxidant activity.

Based on the anti-androgenic activity of this one compound *in vitro*, Applicant claims methods that encompass preventing androgen-dependent prostate cancer, in a human patient, with structurally related compounds.

The specification also provides no direction or guidance for determining the particular administration regimens (*e.g.*, dosages, timing, administration routes, etc.) necessary to prevent androgen-dependent prostate cancer with the compounds encompassed by the claims, particularly in humans. The direction concerning treating prostate cancer is found in the specification at pages 37-44, which merely provides cellular assays for determining the cell growth inhibitory effect of one compound of the invention (PMCol). An *in vivo* assay for determining the efficacy of the claimed compounds using an LNCaP xenograft model is provided at pages 50-52. No compounds were actually tested in this assay. Applicants describe formulations at pages 24-30. No doses useful in preventing prostate cancer in human patients are provided. Applicant asserts that “optimum effective amounts can be readily determined by one of ordinary skill in the art using routine experimentation” (page 24, lines 17-18). However, considering the broad scope of the claimed compounds, it would not be “routine” to determine effective doses of the claimed compounds in human patients.

As noted *supra*, there is both an *in vitro* cellular assay and an *in vivo* assay described at pages 37-44 and 50-52 (with no data in the *in vivo* assay) and it is unclear if these assays correlate to the prevention of prostate cancer in human patients. There is no working example of prevention of androgen-dependent prostate cancer in a human patient using the claimed compounds. Thus, there are no working examples correlating

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inhibition of the androgen receptor in cells with efficacy in the prevention of prostate cancer using the claimed compounds (*i.e.*, Applicant has not shown that inhibition of the androgen receptor with a compound of the invention correlates to *in vivo* prostate cancer prevention with the same compound).

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed genus of compounds could be predictably used as a prevention for androgen-dependent prostate cancer as inferred in the claims and contemplated by the specification.

*Genentech Inc. vs. Nova Nordisk* states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

In the instant case, Applicants have presented a general idea that because PMCol has anti-androgenic activity *in vitro*, PMCol and compounds related to PMCol must therefore, *a priori*, be useful in the prevention of androgen-dependent prostate cancer in human patients. Determining if any particular claimed compound would prevent prostate cancer in humans, would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials or to testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited

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guidance and direction provided by Applicants, especially in view of the fact that there is no known chemical agent that is effective in preventing prostate cancer *a priori*.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-2 and 5-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **Gunawardena *et al.*** (The Prostate, 2000, vol. 44, pages 287-295) (cited by

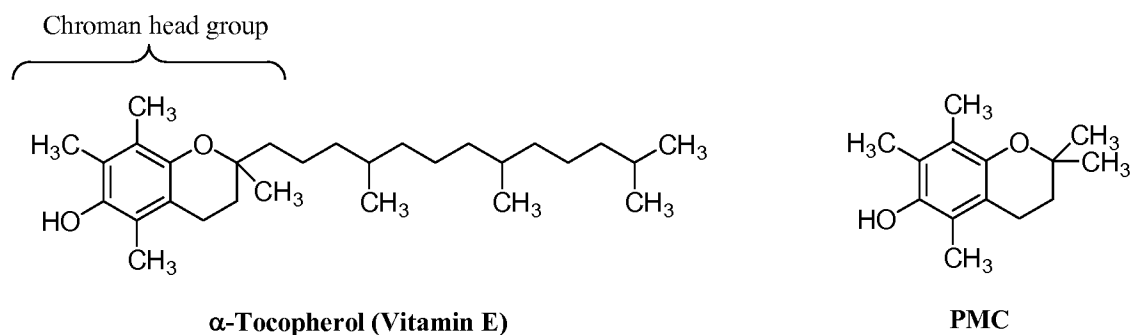
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applicants) in view of **Sheu *et al.*** (Life Sciences, 1999, vol. 65, pages 197-206) (cited by applicants).

Gunawardena *et al.* disclose that vitamin E ( $\alpha$ -tocopherol) and other antioxidants inhibit the growth of human prostate cancer cells through apoptosis (Abstract). The authors disclose that antioxidants have been associated with a reduced risk of cancer in various tissues, including the prostate (page 288, left column). Three prostate cancer cell lines, DU-145 (androgen-unresponsive), LNCaP (androgen-responsive) and ALVA-101 (androgen moderately responsive) were used to test the effects of several antioxidants, including  $\alpha$ -tocopherol on cell growth in culture (*id.* at right column).  $\alpha$ -Tocopherol produced significant growth suppression of ALVA-101 and LNCaP cells compared to control (page 289, left column). The authors further disclose that androgens increase oxidative stress in androgen-responsive but not androgen-unresponsive cells such as PC-3 (page 292, left column). Vitamin E did not cause growth inhibition of in the androgen-unresponsive (DU-145) human prostate cancer cell lines, whereas it did significantly affect the growth of the androgen-responsive cell lines (*id.*). In summary, the authors conclude that the results suggest that antioxidants may retard human prostate cancer cell growth through mechanisms that activate apoptosis (page 292, right column).

Sheu *et al.* compare the activities of  $\alpha$ -tocopherol and PMC (2,2,5,7,8-pentamethyl-6-hydroxychromane) on platelet aggregation and antioxidant activity (Abstract). PMC is the same compound recited in instant claims 2 and 6 and is disclosed to be a “potent antioxidant derived from  $\alpha$ -tocopherol” (Abstract).

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PMC is more hydrophilic than other  $\alpha$ -tocopherol derivatives and has potent radical scavenging activity (page 198). It is also taught in Sheu *et al.* that PMC is a potent inhibitor of nuclear factor- $\kappa$ B (NF- $\kappa$ B) activity (*id.*). PMC was shown to have greater antioxidant activity than  $\alpha$ -tocopherol (page 204). The authors conclude that the antioxidant activities of PMC in various radical-mediated pathological events, particularly in *in vivo* situations, should be further studied (page 205).

It would have been *prima facie* obvious to one of ordinary skill in the art to administer PMCol to patients having androgen-dependent prostate cancer. This is especially true given the correlation between anti-oxidant activity and inhibition of prostate cancer cell growth as taught in Gunawardena *et al.* (*i.e.*, oxidative stress induced by androgens in prostate cancer cells). Accordingly, the skilled artisan would have been highly motivated to administer the instantly claimed PMCol to prostate cancer patients, based on the reasonable expectation that structurally similar species usually have the same properties. See, *e.g.*, *Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *Deuel*, 51 F.3d at 1558, 34 USPQ2d at 1214 (“Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would

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ordinarily contemplate making them to try to obtain compounds with improved properties.”). In this case, PMCol is a more potent anti-oxidant, inhibits NF- $\kappa$ B, and is more hydrophilic than  $\alpha$ -tocopherol. Since  $\alpha$ -tocopherol inhibits androgen-dependent prostate cancer cell proliferation, the skilled artisan would predict, *a priori*, that a compound that is a better anti-oxidant, more hydrophilic, and that also inhibits NF- $\kappa$ B would be as effective, if not more effective, than the parent compound  $\alpha$ -tocopherol in inhibiting androgen-dependent prostate cancer cell growth.

The skilled artisan would have been motivated to administer PMCol (PMC) to patients having androgen-dependent prostate cancer because the prior art teaches that PMCol is a known derivative of  $\alpha$ -tocopherol having potent anti-oxidant activity and that  $\alpha$ -tocopherol inhibits androgen-dependent prostate cancer cell growth *in vitro*, likely due in part to its anti-oxidant activity. The skilled artisan would recognize that the anti-oxidant activity of  $\alpha$ -tocopherol is due to its chromanol head group as evidenced by Sheu *et al.* Further, the fact that  $\alpha$ -tocopherol only inhibited androgen-dependent prostate cancer cell lines would lead the skilled artisan to believe that  $\alpha$ -tocopherol may have anti-androgenic activity in addition to its anti-oxidant activity.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

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Customer Service Representative or access to the automated information system, call

800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/  
Examiner, Art Unit 1614

/Ardin Marschel/  
Supervisory Patent Examiner, Art Unit 1614